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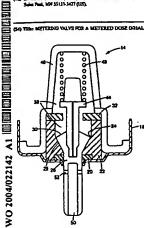
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50 TID: METERING VALVE FOR A METERED DOSE DHALER PROVIDES CONSISTENT DELIVERY



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#### METERING VALVE FOR A METERED DOSE INHALER PROVIDING CONSISTENT DELIVERY

# Background

Metering valves are a common means by which serosals are dispersed from crossi containers. Metering valves are particularly useful for administraine medicinal formulations that include a liquefied gas propellent and are delivered to a patient in an

When administrating medicinal formulations, a dose of formulation sufficient to produce the desired physiological response is delivered to the patient. The proper redetermined amount of the firmulation must be dispersed to the patient in each successive doss. Thus, any dispensing system must be able to dispense doses of the medicinal formulation accurately and reliably to help assure the safety and efficacy of the

Metaing valves have been developed to provide control over the dispensing of medicinal accessi formulations. A metering valve may be used to regulate the volume of a medicinal frequestion passing from a container to a metering chamber, which defines the maximum amount of the formulation that will be dispersed as the pext does. Reliable and controllable flow of the medicinal formulation into the metering chamber may contribute to the accuracy and/or precision of the metering of successive doses of the firemulation. Time, reliable and controllable flow of the medicinal formulation into the metering chamber may improve performance of the metering walve and, therefore, may be highly

In some metering valves, the metering chamber fills with the meticinal formalistics prior to the periors actuating the valve stem and thereby releasing the dene. The metaring chamber is refilled with formulation after dispensing one does so that the matering valve is ready to discharge the next does. Councemently, the metering chamber countins familiation at all times except the the baief time during which the valve stem is depres by the user to discharge a dose. Also, the passageways through which the formulation and fow to make the menting chamber are often marrow and termons. As a result, mercing valves configured in this way have a comber of disadvantages resulting in, for

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example, certain dosing due to less of prime. "Loss of prime" mores the occurrence of vapor or air voids in the metared volume, thereby leading to a shortfull in the volume of dose being metered by the valve. A principal cause of loss of prime is the presence of restrictions in the entry passagoway or passagoways Corough which formulation must puts to 50 the metering chamber. Such restrictions can lead to flow discription and thus also to the occurrence of vapor or air voids in the metering chamber.

Another phenomenon that one lead to creatic dosing is less of dose. "Loss of dose" means a change in the amount of suspended drug or excipient particles in a metered dose of formulation, compared to the average composition of the bulk formulation in the container. A principal cause of loss of does is the settling of drop particles into, or their movement out of, restricted regions of the metaring valve such that the proper concentration of formulation cannot subsequently be obtained within the restricted regions prior to dose delivery. For example, drug particles may actile in a residual metering volume - any part of the messeing valve bounded by a messeing surface and that, when the metering valve is in the resting position, remains fluid filled but is not in substantially freeflowing communication with the bulk formulation.

In other metering valves, residual metering volume may be limited to some extent by designing the metering walve so that the metering chamber does not materialize unless and until the valve stem is actuated. However, even in these metering valves, a small praidual pratering volume exists when the metering valve is street because a small amenter gap exists between the valve arem and the metering valve body.

Actuation of these valve stems can be divided into a filling stage and a discharge stage. The filling stage begins as the valve sum is depressed during actuation. The action of depressing the valve stem causes the finemation of a transient matering chamber, which is in finid communication with the residual metering volume defined by the small ampula gap. As the valve earn is depressed, the transient purties of the metering chambes expends and flumulation enters the metering chamber. As displacement of the valve man continues, a stage is reached at which filling of the transient metering chamber steps.

Eventually, displayment of the valve stars continues to the discharge stage, in which the meteral formulation is discharged. In these valves, a single setuction thus causes aspid filling of the transient metering chamber followed by discharge of the

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formation to the patient. Generally, noticed formulation does not uside for any approximate length of time in the metering chamber in these metering valves. However, some formulation may reside in the residual metering volume defined by the small enumber gap when the metering valve is at real.

Some metaring valves limit the bright of the attenter gap, thereby reducing the residual volume and limiting the amount of formulation that residue in the metering chamber between actuation ovents.

While a metering walve having a transient metering chamber provides advantages over other types of metering valves for the delivery of second formulations, the flow of formulation from the constants to the metering chamber may be disrupted. Disrupted flow of formulation retire to filling a metering chamber through one or more bottleneck regions of significantly restricted scores. Flow disrupt the bottleneck regions may be impeded enfliciently to give rise to substantially incomplete filling of the metering chamber, particularly under conditions typical of patient use. When this happens, formulation may be delivered in inconsistent or inaccounts dones. Of course, all metering chamber inlets become significantly restricted immediately prior to being scaled off during actuation. Disrupted flow, so just descended, refers to flow secons during the majority of the filling stage of stantation.

Centrin neturing valves have been designed to improve the flow of farmulation into the metering chamber. For example, some metering valves include angled spillway filling chamnels designed to himit disruptions of the flow of formulation into the metering chamber. Less disrupted flow may decrease the likelihood and extent to which vapor or air voids form in the meterod volume and, therefore improve performance of the metering valve.

### Summary of the Invention

The present invention relates to a novel design for a metering valve that provides improved consistency of formulation delivery. The metering valve of the present invention includes a valve stem designed to (1) limit or climinate the residual metering volume, thereby reducing the smooth of formulation that resides in the metering chamber while the meeting valve is at rest, and (2) limit tenticions on the from flow of formulation

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FIG. 11 is an embrgod cross-excitonal view of an alternative embodiment of a valve stan according to the present invention.

FIG. 12 is an enlarged cross-sectional view of mother alternative embodiment of a valve stem according to the present invention.

## Detailed Description of the Invention

The following description is set forth to terms of an seronal metering valve used to dispense as served formulation from an acrosal container. However, the metering valve and methods of the present invention have application to virtually any presentant fluid municipal delivery of an accumate, method does. In particular, the metering valves described herein are useful for dispensing medicinal seronal formulations.

When used to dispense moticinal acrosof formulations, a metering valve according to the present invention may be used to administrat virtually any acrossis formulation of drug into a body cavity of a patient, such as the month, none, usus, vagina, cars, or onto the eyes or any state error of the patient. However, the present invention is not limited to medicall applications and may be used whenever a prectice amount of material from a measurant fluid is to be delivered to a given region.

FIG. 1 shows an acrossed dispositing appearants, grosselfly designated as 10, that incorporates one embodiment of a metaring valve 14 according to the present invention. The top and of the metaring valve 14 is entimped around the end of a conventional according to the present inventional discharge piece 16 is mounted around the bottom of the metaring valve 14. Thus, accord formulation is dispossed downweathy from the acrossed container 12, through the metaring valve 14. Can through the discharge piece 16 where it is differed to a patient. The discharge piece 16 directs the acrossed formulation toward the body cavity or dain sens to which the formulation is to be delivered. For example, discharge piece 16 may be a monthpiece that can be inserted into the patient's mouth, thereby providing and administration of the across formulation.

The sensed-dispensing device shown in FIG. I is merely one example of how a necturing valve according to the present invention can be incorporated into a dispensing operation. Purchamora, the configuration of the discharge piece 16 depends upon the application for the sensed.

into the metering chamber. Consequently, consistent delivery of flammlation is obtained by reducing the effects of loss of prime and loss of dose.

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The present invention provides an acrosol matering valve that includes a valve stem that generally defines a longitudinal axis, a valve body, and a incturing gesters configured to be able to form a transient, substantially finid-tight fines seal between the valve term and a scaling portion of the valve body. The valve stem includes a body portion including a proximal end, a distal end, and at least one tide surface connecting to proximal end and the distal end and including a metaring surface, wherein the longitudinal exist and a phase tangential to at least a portion of the matering surface define an engis from about 2° to about 50°.

#### Brief Description of the Drawings

FIG. 1 is a cross-sectional view of a metered does inhalor including an embodiment of the across exetering valve according to the present invention.

FIG. 2 is an embrand cross-sectional view of one embodiment of another serosol metering valve according to the present invention in the resting position.

FIG. 3 is an embarged cross-sectional view of the acrossol metering valve shown in FIG. 2 during the filling stage of valve stem actuation.

FIG. 4 is an enlarged cross-actional view of the across luncturing valve shown in 20 FIG. 2 at the filled stage of valve error actuation.

FIG. 5 is an enhanced cross-sectional view of the acrossel metering valve shown in FIG. 2 during the discharge stage of valve stem schasion.

FIGS. 6 and 7 are enlarged cross-sectional views of the embodiment of an acrossle metating valve shows in Figure 1 in the resting position and during the discharge stage of the valve stam actuation, respectively.

FIGS. 8 and 9 are enlarged cross-sectional views of a further embodiment of an acrosol meaning valve according to the present invention in the resting position and during the discharge stage of the valve stem actuation.

FIG. 10 is an enlarged cross-sectional view of one embodiment of a valve stem according to the present invention.

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In many of the figures, a metering valve or valve stem is shown in isolation for case of illustration. The valve stems shown in isolation may be combined with one or more additional components to form a metering valve. Such metering valves, as well as metering valves shown in isolation in the figures, may be combined with one or more additional components to form on serousd dispensing device. It is understood that any particular ficture shows in a metering valve and/or valve stem combodiment may be combined with fixtures shows in other embodiments and/or incorporated appropriately within other embodiments.

Refuring to FIG. 2 showing an embodiment of a metering valve 14 (in the sesting position), the metering valve 14 typically includes a housing 18 that serves to house the various components of the metering valve 14. The top portion of the housing 18 stoches to the servest contrainer 13 (as exemplately shown in FIG. 1). A valve body 22, typically sexted within the valve housing 18, in turn provides a housing for a valve stem 24. The valve houly 22 includes an interior surface 24 defining an internal chamber or cavity of the valve body.

The metaring valve 14 typically includes a quing cage 46 thus, together with the valve body 22, defines an interior chamber 33, a portion of which is occupied by a portion of the valve stem 26. One or more inlets (not shown) typically traversing the spring cage provide open and unrestricted fluid communication between the interior chamber 38 and the across complete 12.

The vatve sum 24 includes two portions, a body portion and a stum portion. The sum portion includes that portion of the valve sum that is conside the valve boosing 18 when the valve stum 26 is in the resting position shows in FIG. 2. During actuation of the valve sum 24, however, the sum portion will be displaced inwardly with respect to the metasing valve 14, as described more fully below, so that some of the stum portion will be unstantly positioned inside the valve housing 18. The stem portion belotes a passageway 50 through which a metered does of themshrine is discharged, as will be described more fully below. The passageway includes one or more side bokes 52.

The body portion of the valve stran 15 is that portion that is positioned within the valve bossing 18 throughout schesion of the valve stran 15. The body portion of the valve stran 15 (as shown in FKCS, 2-5) includes a measuring scribe; 28 and a making scribe; 20.

The body portion of the valve stem 26 is configured to have substantially the same chape as the eurocucling wall of the valve body 22. Thus, as can be seen in the embediment shows in FIG. 2, a substantial parties of the metaring surface 28 of valve men 26 cests in counset with the interior surface of the valve body 24 when the metering valve is in the resting position, thereby minimizing, if not eliminating, the annular gap between the valve stem and valve body when the metering valve is in the resting position. and thus minimizing, if not eliminating, residual metering volume.

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The metering valve may include a spring guide 44 mounted on the end of the valve stem body portion opposite the stem portion and a spring 48 within the interior chamber 38 of the motoring valve as shown in FIG. 2. The spring 48 through consequences with the spring guide biases the valve stren 26 toward the resting position. It will be approximated by those skilled in the set that any smitable mount for biasing the valve stem 26 into the resting position, e.g. coil compression spring or a spring appropriately mounted external to the interior chamber, may be used in connection with metering valves according to the persent invention. The spring guide easy be an integral part of the valve stem and/or arranged to include a pressure filling ring as described in the US Patent US 5,400,920, which is incorporated by reference berein.

The pretering valve 14 also includes at least two angular garkets, the displacem 20 and the matering gardest 32. The disphrasm 20 is positioned between the valve housing 18, the valve body 22 and the valve stem 26, as shown in FIG. 2. The displangm 20 isolates the formulation in the aerosol container 12 from the exterior of the valve by faming two finid tight scale: 1) an annular sliding scal between the disphragm 20 and the valve stem 26 where the valve stem extends out of the valve housing, and 2) two compressive planar or face scale between the valve body 12, the disphrasm 20 and the housing 18. The latter seal may be effected either with or without a scaling bead on either the valve body 22 or the housing 18.

In the canhediment shown in FEGS, 2-5, the metering gasket 32 is included in the body wall of the valve body, being generally positioned between the valve body 22, the spring cases 46, and the body portion of the valve stem 26. The metering gasket 32 forms two finid tight compressive planer or face scale between the metering gaslert 32 and the

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mber 38, the formulation persons between the spring guide 44 and the metroing guidet 32. Formulation flows around the proximal end of the valve stem 26 between the valve stem 26 and the interior surface of the valve body 24 and enters the expanding metering chamber 34. The spring guide may be provided with cut-away portions or openings to improve flow and/or access to the metering chamber.

Thus, as the valve surm 26 is moved from the resting position shown in FIG. 2 to the filling stage shows in FIG. 3, excessed formulation passes from the aerosol container 12 to the metering chamber 34 immediately upon actuation of the valve stem 26. Formulation ues to fill the metering chamber 34 until the metering valve 14 reaches the filled stage as depicted in FIG. 4. As will be described in more detail below, the flow of formulation into the metering chamber 34 may be affected by the angle described by the metering surface of the valve stem 28 with respect to the octobal longitudinal sxis of the valva stran

At the end of the filling stage, the flow path of formulation from the acrosol combiner 12 to the metering chamber 34 is out off as the metering garket 32 contacts the scaling surface 30 of the valve stem 26, as can be seen in FIG. 4. The metering gashet 32 forms a fluid-right, then seal with the sealing nurhers 30, thereby concluding filling of the metering chamber 34 and isolating the metering chamber prior to discharge. The scaling surface 30 may be provided with a scaling bead and may be any shape suitable for providing desired scaling characteristics. However, for enhanced scaling performance and value conversion, as discreted in more detail below, the sestion surface 30 is desirably generally conical and more particularly in its longitudinal cross-section the sides may be either anhenemisly straight-edged (as shown in e.g. FIGA) or conceive (as shown in e.g.

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At this stage, the metered dose of formulation is isolated and ready for discharge from the metering chember 34 and delivery to the patient. The dimensions of the valve body 22, valve som 26 and other valve components determine the filled-volume of the metering chamber 34 in the completely filled position.

FIG. 5 depicts the metering valve 14 in the discharge stage of actuation. In order to discharge the meteod dose of secretal forestation from the metering chamber 34, the valve soon 26 is further acrossed to the precision illustrated in FIG. 5. Those deilled in the

valve body 22 and the spring cage 46. Them may be achieved either with or without a scaling bend on the valve body 22 and/or the spring cage 46.

The metering gasket in this embediment or other embediments in accordance with the persons invention may be either mechanically affixed, molded own the respective empenent of the metering valve, or the respective components may be mounfactor using, for example, a two shot or co-molding process in which the convexpositing next of the metering valve and metering gratest are co-molded so that a strong bond (mechanical and/or chemical) can be achieved between the components.

As shown in FIG. 4, the metering grades 32 transiently isolates the formulation in the metering chamber 34 from the serosol container 12 by farming a fluid-tight face seal between the metering grades 32 and the scaling surface 30 of the valve storn 26. The metering gasket 32 provides a means for terminating the flow of formulation from the served container 12 to the metering chamber 34 during actuation of the valve stem 26, as will be described in more detail below.

Operation of the metering valve 14 shown in FIG. 2 is illustrated in FIGS. 3, 4 and 5. The figures illustrate the stages of operation of the metering valve 14 and the corresponding relative positions of the valve components so a patient actuates the valve stem 26, thereby releasing a dose of acrosol flumbation. FIG. 3 shows the metering valve 14 in the filling stage, FIG. 4 shows the metering valve 14 in the filled stage, and FIG. 5 shows the motoring valve 14 in the discharge stage.

As can be seen in FIG. 3 during the filling stage of actuation, the valve stern 26 has been displaced inwardly into the interior chamber 38 against the compressive force of the spring 48. As the valve stem 26 is displaced inwestly, the proximal end of the stem portion of the valve stem 26 enters the valve housing 18. As a result, a metering chamber 34 is formed between the interior surface of the valve body 24 and the meterior surface 28 of the valve stran 26. The volume of the metrains chember 34 increases as the valve stran is displaced until it reaches its filled-volume at the end of the filling steem as denicted in FIG. 4 showing the completely filled position.

Acrosol formulation enters the filling volume of the metering chamber 34 in the following meaner. Possulation from the acrosol container 12 passes through the one or more inlets and into the interior chamber 38 of the meterine valve. From the interior

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art will realize that the distance traveled by the valve stem 26 between FIG. 4 and FIG. 5 will result in an expansion of the metering chamber 34 without increasing the metered dose. The extra travel ensures that the metering gasket 33 is scaled against the scaling surface 30 before the one or more side holes 52 enter the metering chamber 34. As can be appreciated from FRGS. 4 and 5, as the valve stem is further actuated from the comp te de la filled-position (as shown in FIG. 4) to the discharge position (illustrated in FIG. 5), the metering easier 37 stretches and the facing contact surfaces of the metering grainst and the scaling surface 30 show a relative movement to one another in reciprocation of the travel of the valve street. Thus the face seal here may be considered a dynamic, reciprocating face scal. As the valve stran 16 is fully actuated, the one or more side bokes 52 of the discharge passageway 50 pass through the displanges 20 and come into finid communication with the metering chamber 34. The fluid communication thus established allows the ser formulation within the metering chamber 34 to be released into the one or more side holes

During the discharge of the second formulation from the metering chamber 34 as shown in FIG. 5, the metering gasket 32 continues to provent the passage of additional bulk fermulation from the seroeol container 12 to the metering chamber 34, with allowence made for the dimensional telepances of the valve components. After the does of narrows formulation is discharged, the patient releases the valve stem 26, which returns to its priginal creating specials demicted in FIG. 2 by at least the biasing action of the spring 48. In some embodiments, the metering grades 32 also may provide biasing action that promotes comm of the valve stem 26 to the resting position.

52 and the formulation than pusses through the discharge passageway 50, thereby

delivering the metered dose of seronal formulation to the patient or other desired area.

The autocessive stages of valve stem actuation, as exemplarily depicted in FIGS. 3, 25 4 and 5, are all accomplished during the brief duration of actuation of the valve stren. Accordingly, formation, filling and emptying of the metaring chamber occurs rapidly. At most, only a very small percentage of a dose of freembation resides in the metering chamber between actuations. In some embodiments, the metering chamber cary not exist at all in the resting state - the residual metering volume curry be zero - so that so formatation can reside in the metaring chamber between actuations. Because the etages of valve stem actuation occur rapidly, the metering chamber is full of financiation only for a

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brief moment immediately prior to discharge of the formulation from the metering

FIGS. 6 and 7 illustrates another embodiment of a metering walve 14 in its resting position and during discharge stage of actuation. This embodiment provides an example in which the spring guide 44 is framed of two parts, a spring guide stem 44 and a spring guide stem 44 and a spring guide stem 44 and a straight of the spring guide stem are formed as a single character and the spring guide stem as the spring guide stem and the spring guide stem is framed as a steparate character, which is subsequently affixed octo the spring guide stem.

In comparison to the embodiment of FIGS, 2-5, in this embodiment the body portion of the valve stum 26 is configured such that the angle described by a unjor portion of the maturing surface 28 of the valve stem with neapest to the central longiminal axis of the valve stem is larger. During actuation of the interring valve 14, the operation of which is the same as that described for the embodiment illustrated in FIGS, 2-5, for flow of formulation during the filling stage into the metering chamber 34 farmed upon actuation is further enhanced, as discussed in more detail below, these to the describable configuration of the metering surface 28 of the body portion of the valve stem 26. The scaling surface 39 in this embodiment, similar to the scaling surface in the embodiment depicted in FIGS, 2-5, is also generally context. This embodiment provides an example of a metering valve including a scaling surface 30 which is embodiment provides an example of a metering valve including a scaling surface 50 which is embodiment provides an example of a metering valve including a scaling surface 50 which is embodiment provides an example of a metering valve including a scaling surface 30 which is embodiment provides an example of a metering valve including a scaling surface 50 which is embodiment provides an example of a metering valve including a scaling surface 30 actually generally contexts and a scaling surface 32 against the scaling surface.

FIGS. 8 and 9 illustrate a further embodiment of a metering valve 14 in its resting position and during discharge stage of actuation. This embodiment is similar to the embodiment shown in FiGS. 6 and 7. Sent the body portion of the valve stem 26 is configured such that the sigh demands by a major portion of the metering aucthor 22 of the valve stem with respect to the control longitudinal axis of the valve stem is oven greater, being about 90°, and the scaling surface 30 is generally conical with substantially straight-edged sides in its longitudinal cross-section.

The configurations of the valve body 22, valve stem 26 and in some cases other valve components influence free flow of formulation and the presence of resistnal meterine

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 $\leq$  5 % or more denirably  $\leq$  2.5 %), more aritably as substantial portion (a.g.  $\leq$  2 % or more denirably  $\leq$  1 %), or most satisfyly no portion of the scaling surface adjacent to the intention between the metering surface and the scaling surface of the body portion of the valve body is aligned pseudicl or nearly parallel to the stren axis.

As mentioned above, the flow of fraministion into the metering chember duping actuation may be affected by the engle described by the metering nurface of the valve stem with respect to the central longitudinal state of the valve stem. For example, the valve stem 24 may define a central longitudinal state of as shown in FIU. 10. As maje 8, may be defined by the intersection of a plane 63 temperatual to a major portion of the metering nurface 23 of the valve stem and the central axis of 0, he some embodiments with complex geometries, maje 8, may be defined by the intersection of the central state of 0 and a plane temperatual with a minor portion of the metering surface 22, as shown in FIG. 12.

All class being equal and assuming that the valve body in configured to substantially confirm to the valve term, a larger  $\theta_0$ , results in a wider filling gap for a given displacement of the valve term during actuation of the neturing valve. For given scaling displacement of the valve term during actuation of the metering point, a larger value of  $\theta_0$ , generally allows the valve stem and the metering valve to be shorter. The shape of the metering surface 28 shown in FKJ. 12 allows the use of a particular angle  $\theta_0$  in a shorter metering valve. A simpler metering surface, such as that shown in FKJ. 10, may require less dimensional control to order to meantheture the valve stem and valve body that substantially confirm to one souther and thereby limit or eliminate residual metering wolfme when the metering valve is a rest.

Suitable values the engle 0, in valve stems according to the present invention are from about 2° to about 90°. Within this range a minimum angle of about 10° is more destrable, about 20° even more destrable and about 10° more destrable. A maximum angle of about 80° is more destrable, about 70° even more destrable and about 60° moral

To limit the potential of areas of practical flow within the metaring chamber and then exhaused then flow of formulation into the metaring chamber, the metaring serious is denirably configured to comprise no significant portion (e.g.  $\leq 5$ % or more desirably

volume when the metering valve is in its resting position as well as the flow of formulation into the metering chamber 34 when the valve stem is actuated.

For example, when the metering portion (a portion that, in part, bounds the neturing chamber formed upon actuation) of the valve body is configured to substan comform to the metaring surface of the valve stem, when the metaring valve is in its resting position, the presence of residual metering volume is minimized. Under the term including portion of the valve body is configured to substantially conform to the metaline surface of the valve stem", it is desirably understood that a significant portion (a.g. ≥ 90 %) of the metering surface of the valve stem rests in contact with the interior purface of the valve body when the metering valve is in the resting position. The residual metering volume may be further minimized, by configuring the metering portion of the valve body to executially conform or to conform to the metering surface of the valve stem when the valve is at rest. Under the term "metering portion of the valve body is configured to essentially conform or to conform to the metering surface of the valve stem", it is desirably understood that substantially the complete portion (e.g. ≥ 95 %) or essentially the complete portion (e.g. ≥ 97.5 % or more desirably ≥ 99 %), respectively, of the metering surface of the valve stem rests in contact with the interior surface of the valve body when the metering valve is in the reating position.

Proc flow of formulation in the valve in its rest position may be further desirably influenced, by configuring the meaning surface of the body portion of the valve stem, each that so significant portion (a,  $\xi \le 5$  % or more desirably  $\le 2.5$  %), more satisfy no substantial purson (a,  $\xi \le 5$  % or more desirably  $\le 1$  %), or most suitably no portion of the meaning surface adjacent to the intenthee between the meaning surface and the scaling surface and the scaling surface and the body portion of the valve body is aligned parallel or nearly parallel to the stem axis (i.e., with a very small engle 8, 8,8, 0' or 17). Also, then dowing communication between the bulk formulation and formulation within the interior chamber, in particular in the vicinity of the body portion of the valve stem and the internal chamber or cavity of the valve body defined by the interior surface of the valve body wall, when the meaning valve is in the resting position may be enhanced by certain configurations of the scaling surface of the body portion of the valve stem. In particular, it may be desirable to configure the scaling author of the tody portion of the valve stem, such that no significant portion (a,  $\xi$ 

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 $\le 2.5$  %), more suinbly so substantial parties (e.g.  $\le 2$  % or more desirably  $\le 1$  %), or most suinbly so portion aligned parallel or nearly parallel to the stem exis.

At can be seen in the exemplary embodiments shown in PIGS. 2, 6 and 8, the body portion of the valve stem typically includes a section ediscost to the stem portion, which is aligned parallel or county parallel to the stem exist. This section fleditions the passage of the valve housing and/or the displangen. Because this section is adjacent to the stem portion and at the distral end of the metering chember formed upon extention (as can be appreciated for example in FIG. 3), a parallel or nearly parallel slignment of this section of body portion does not restrict the flow into the metering chamber.

As can be best seen in FRGS. 10 to 12 showing exemplary valve stems, the maturing surface 28 is typically that surface of the section of the body portion located between the section of the body portion comprising the sealing surface 30 and the section of the body portion of the body portion experience in the stem sexis. The circumferential interface or boundary of the metring surface and the stem sexis. The circumferential interface or boundary of the metring surface and the sealing surface may generally be understood to be the summas of widest transverse cross section of the valve stem to body. In embodiments, which is accordance to the aforesaid definition would have an interface or boundary having a portion parallel to the longitudinal sexis of the stem, the interface or boundary is typically understood in this case to be the standards at the proximal end of the parallel portion (i.e. the end distinct from the stem portion). As can be appreciated from FIGS. 10 to 12, if the valve stem includes a mounted or integral spring pride 44, the sealing surface 30 typically cods at the interface or boundary between the surface of the body portion of the valve stem and the surface of the spring pride.

The scaling characteristics end/or the flow of facuntation into the catering chamber thring setuction and/or from flow of facuntation when the nextring valve is at rest may also be effected by configuration of the scaling nuthers, and as mentioned above, the scaling surface 30 is destinably generally consisted and more periodicity in its important of the scaling surface 30 is destinably generally consisted and more periodicity in its important of the scaling scales are either schematically unsign-edged or conserve. The argie described by the scaling surface of the valve stem whe expect to the control lengthedized is the control lengthedized acts of the valve stem may also have an effect.

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Referring to FIG. 10, so engis 0, may be defined by the intersection of a plane 64 temperatal to a major portion of the scaling nurface 30 of the valve scan and the central axis 60. Typical values for engis 0, may be from about 30° to about 50°. Within this range, a minimum angle of about 73° is more destrable and about 40° most destrable. A maximum engis of about 75° is more destrable and about 70° most destrable. In some embodiments, angle 0 about 75° is more destrable and about 70° most destrable. In some embodiments, angle 0, may be defined by the intersection of the central axis 60 and a place temperatural with a minor portion of the scaling surface 30. For embodiments in which the scaling surface is generally conical in form with concave sides in its longitudinal cross-section, angles of 0, may be defined along the entire concave surface by the intersection of the central axis 60 and planes temperatis in the curved surface; the values of these angles are destrably all within the sanger defined above.

Memoring valves having an angle 0<sub>6</sub> in the names described may have a metering portion - a portion that, in part, bounds the metering chamber - that one generally be described as contical in shape with a cross-sectional area of the proximal protect of the cone. In some embodiments, the tensaverse cross-sectional area of the valve stem body at the memoring and saling author interface may be about 4% greater than the transverse cross-sectional area of the valve stem body at the memoring area of the distal end (i.e. towards the stem portion of the valve stem) of the valve stem body. In other embodiments, the transverse cross-sectional area of the valve stem body at the metering and sealing surface interface may be at least about 20% greater than the transverse cross-sectional area of the distal end of the valve stem body, in still other embodiments, the transverse cross-sectional area of the distal end of the valve stem body, in still other embodiments, the transverse cross-sectional area of the distal end of the valve stem body at the metering and scaling surface interface may be at least about 60% greater than the transverse cross-sectional area of the distal end of the valve stem body.

In certain embodiments having a generally conical metering portion, the interior surface of the valve body maintains a generally conical form from the displanger to the valve body scaling surface.

The meturing number 28 of the valve stars 26 may be of any minoble configuration and still define the plane 62 used to define angle  $\theta_{\rm w}$ . For example, in a valve stars having relatively simple geometry, such as the valve stars shown in FIG. 10, a majority of the meturing surface 28 may define the plane 62 used to define angle  $\theta_{\rm w}$ . Alternatively, the

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of the present invention may be used to conjunction with general metering valve designs other than those explicitly shown in the Figures. Such alternative metering valve designs may include one or more additional fratures of the valve steam, valve body, or any other persons of the metering valve designed to improve performance of the metering valve. Such additional design features may improve metering valve pershamance by improving performance parameters including but post limited to formulation flow from the served container to the metering chamber during actuation and consistency of farameterion

Various modifications and alternations to this inventions will become apparent to those skilled in the set without departing from the scope and spirit of this invention. It should be understood that this invention is not intended to be underly limited by the about the understood the this invention is not intended to be underly limited by the literarchy comboliments and examples set forth herein and thus one examples and embodiments are presented by way of examples only with the scope of the invention intended to be limited only by the claims set furth herein as follows.

metering surface 28 may be irregular, such as is shown in FIGS. 11 and 12, and only a portion of the metering surface may be used to define the phone 62. Additionally, irregularities in the metering surface 28 may be one-geometrical and still provide a suitable confirmation for valve stem 16 according to the cream invention.

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Thus, the perticular geometry of the metering surface 28 is not critical so long as (1) anglo 0, can be defined as described herein, (2) the interior surface 14 of the valve body 13 is configured to substantially confirm to the geometry of the metering surface 18. These factors contribute to limiting or eliminating residual metering woltmap when the metering valve is at rest and facilitate the reduction of restriction of the flow of formulation to the metering chamber. Furthermora, it may be advantageous for limiting or eliminating residual metering valves to significant periods of the metering surface and/or the staling surface and/or the staling surface and the seating surface is aligned perallel or housty parallel to the stem axis. The metering surface may be configured to have no significant or substantial portion or more desirably, no perion aligned perallel or nearly parallel to the stem axis. This may contribute to limiting the formation of stress of restricted flow within the metering chamber and then restriction on the five of five aligned perallel or nearly parallel surface metering chamber and then restriction on the five of the metering chamber are one though the interior surface 24 of the valve body 22 substantially confirms to the geometry of the metering surface 24.

Simple geometries the the metering surface 18 and the interior surface 14 of the wave body may provide octain meantheturing advantages. For example, valve strons having complete 560° recutional symmetry require on rotational alignment during valve essentially. Simple shapes such as oones might also confir ortational alignments during valve resembly. Simple shapes may reduce problems with deposition of drug or with formulation flow discontinuities at engular edges. However, more complex geometries also are satisfied for valve seems 16 secording to the present invention. Per example, some embodiments may include beautyphetrical or other curved configurations. Other embodiments may include walve stems having multiple angles, such as those shown in FRGS. 11 and 12.

The design of the metering surfaces according to the present invention may compliant, along with other aspects of metering valve or valve stom design, to improve the flow of flumniation through the metering valve during actuation. Accordingly, the designs

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What is Claimed is:

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1. An acrosol metering valve comprising:

(a) a valve stem that generally defines a longitudinal sxis and comprises:

(1) a body partion comprising a proximal end, a distal end, and at heat one side surface connecting the proximal end and the distal end and comprising a metaring number, wherein the longitudinal axis and a plane temperatial to at least a parties of the metaring surface define an angle from about 7° to about 90°, and

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(2) a stem portion comprising a discharge passageway,

(b) a valve body comprising:

(1) a body wall that comprises a scaling portion,

(2) an internal chamber defined at least to part by the body wall and comprising a metering portion configured to substantially confirm to the motoring surface of the velve stem, and

(3) a displangen having with that define an operators in stickblo, sealing engagement with the stem portion of the valve stem; and

(c) a metering gasket configured to be able to from a trinsient, ambatumially fluidtight face seal between the valve stem and the scating portion of the body wall.

 An accord metaring valve according to chim 1, wherein the body wall scaling purtion comprises the metaring grates, which is configured to be able to from a transient, substantially fluid-tight three scal with at least a purtion of the proximal end of the valve stam body.

3. An acrossol mentaing valve according to chrim 2, wherein the body portion of the valve stem comprises a scaling author edipons to the meaning surface and distant from the stem portion of the valve stem and wherein acid scaling surface and the matering author them a circumfirential interface on the surface of the valve stem body portion.

 An errorol matering velve according to claim 3, wherein no significant portion of the metering author enclose the scaling number of the valve sum adjacent to the interthed

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between the matering curface and the scaling surface is aligned parallel or nearly parallel to the longitudinal exis.

- An across) metering valve according to claim 3 or 4, wherein the scaling nurther is
   generally conical or covical.
  - An acrossol metering vulve according to claim 5, wherein the sides of the scaling surface in its longitudinal cross-section are substantially straight-edged or straight-edged.
- An across) metering valve according to claim 5, wherein the sides of the scaling amface in its longitudinal cross-section are unbatantially concave or concave.
- An acrosol metering valve according to any of claims 3 to 7, wherein the longithdinal axis and a plane tragential to at least a portion of the seeding surface define on 13 angle from about 30° to about 80°.
  - An acrossi metering valve according to any proceeding claim, wherein the metering surface is generally conical or conical.
- 20 10. An acrossi metering valve according to any proceeding claim, wherein the angle of the metering surface is equal to or greater than about 10°.
  - 11. An acrosol metering valve according to any proceeding claim, wherein said angle of metering surface is equal to or greater than about 20°.
  - 12. An aerosol metering valve according to any preceding claim, wherein said angle of metering surface is equal to or greater than about 30°.
- An accord metering valve according to any preceding of claim, wherein said angle
  of motoring surface is equal to or less than about 50°.

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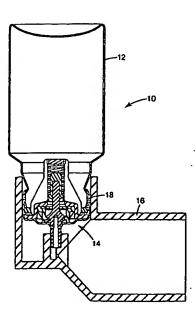


Fig. 1

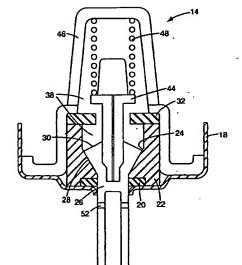
- 14. An exceed metering valve according to any proceeding of chain, wherein and angle of metering surface is equal to or less than about TO\*.
- An aerosol metering valve according to any proceeding of claim, wherein said ample
   of metering surface is equal to or less than about 60°.
  - 16. An extraol netering velve according to any proceeding claim, wherein the metering surface comprises no significant portion eligned parallel or nearly parallel to the longitudinal axis.
  - A metered dose dispensing device comprising an across metering valve according to any proceeding claim.
- A metered dose dispensing device according to claim 17, wherein said metered
   dose dispensing device is a metered dose inhalor.

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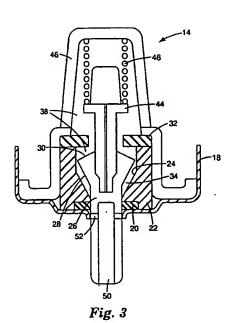
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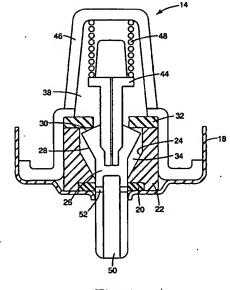


Fig. 4

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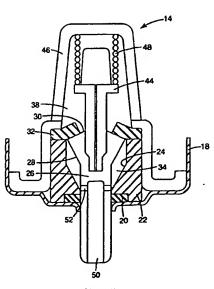
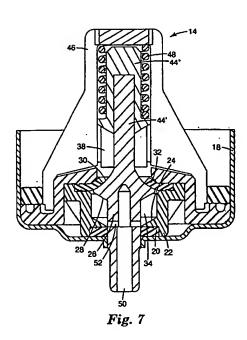
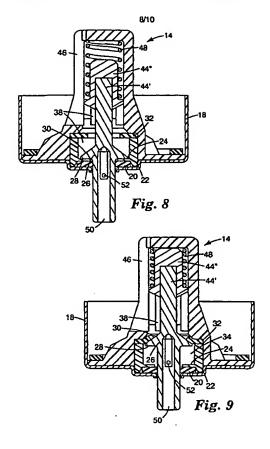


Fig. 5

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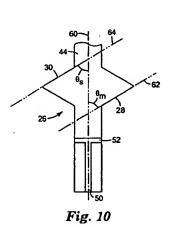


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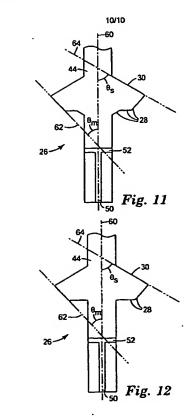
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A	the whole document			1-3,5,7,			
			1	9-17			
Y i	US 4 819 834 A (THIEL CHARLES 6)	18					
	13 April 1989 (1989-04-11)	-					
A	the whole document	1-17					
y I	US 5 169 038 A (DI GIOVANNI PATRI	i	1-3.9-17				
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page 1 of 2

Public distribution	INTERNATIONAL SEARCH REPORT				PCT/US 03/27587	
18 1201918 A 12-08-1970 BE 1201919 A 12-08-1970 BE 1301919 A 130-08-1990 BE 1301919 A 130-08-1990 BE 1301919 A 130191 A 1301919 A 130191 A 1301919 A 130191 A 1301919 A 130191 A 1301919 A 130191 A 1301919 A 13019 A 1301919 A 1301919 A 1301919 A 1301919 A 13019 A 13019 A 13019 A 13019 A 13019 A 13	Picers document	Т	Patradon data		Petrot facily pactor(s)	Publication
US 4819834 A 11-04-1989 AU 620253 62 13-02-1992 AU 6207790 A 06-12-1990 AU 6207790 A 06-12-1990 AU 7811687 A 17-03-1988 CA 1281012 C 05-03-1991 OI 3776843 OI 02-04-1992 EF 0260087 A2 16-03-1993 JP 2612865 62 21-03-1997 JP 6307696 A 07-04-1988 JP 2612865 62 21-03-1997 JP 6307696 A 07-04-1988 KR 9601236 81 24-01-1996 US 5169038 A 08-12-1992 FR 2570139 A1 12-04-1995 EF 0551782 A1 21-07-1993 JP 3467629 02 17-11-2003 JP 5254578 A 05-10-1993 US 4427137 A 24-01-1984 IT 1114362 8 13-08-1986 FR 2694730 A1 21-08-1986 FR 2694730 A1 21-08-1986 FR 2694730 A1 21-08-1986	B 1201918	A				
AU 6207790 A 06-12-1990 AU 60428 B2 20-12-1990 AU 60448 B2 20-12-1990 AU 7811687 A 17-03-1988 CA 1281012 C 05-03-1991 DI 3776843 D1 02-04-1992 EF 0250087 A2 16-03-1983 JP 2612855 B2 21-03-1997 JP 63076966 A 07-04-1988 KR 9601236 B1 24-01-1996 CF 62701391 D1 24-03-1995 DI 62701391 D1 24-03-1995 DI 62701391 T2 11-04-1996 EF 0551782 A1 21-07-1993 JP 3467629 B2 17-11-2003 JP 5254578 A 05-10-1993 US 4427137 A 24-01-1984 II 1134362 B 13-08-1986 EF 1249139 A1 119-08-1982 EF 2494390 A1 21-05-1982	8 1035304	A	06-07-1966	DE	1450502 A1	22-05-1969
AU 504498 02 20-12-1990 AU 7811687 A 17-03-1988 CA 1281012 C 05-03-1991 DE 3776843 D1 02-04-1992 EF 0250067 A2 16-03-1993 JF 2612855 02 21-03-1993 KR 9601226 81 24-01-1996 KR 9601226 81 24-01-1996 DE 69201391 D1 24-03-1995 D1 69201391 D2 24-03-1995 D1 69201391 D2 24-03-1995 D1 69201391 D2 24-03-1995 D2 37264782 A1 12-04-1996 D2 37264782 A1 12-04-1996 D3 4427137 A 24-01-1994 II 1114482 8 13-03-1996 D2 3126510 A1 19-03-1996 EF 244279 A1 13-03-1996 D2 3126510 A1 19-03-1996 EF 244279 A1 13-03-1996 D2 3126510 A1 19-03-1996 D3 3126510 A1 19-03-1996	US 4819834	A	11-04-1989			
AU 7511467 A 17-03-1988 CA 1281012 C 05-03-1991 OI 3776843 OI 02-04-1992 EF 0250057 A2 16-03-1993 JP 2612865 B2 21-03-1997 JP 63076996 A 07-04-1988 KR 9601236 B1 24-01-1996 US 5169038 A 08-12-1992 FR 2670139 A1 12-06-1995 EF 0551782 A1 21-04-1996 EF 0551782 A1 21-04-1996 EF 0551782 A1 21-07-1993 JP 3467629 B2 17-11-2003 JP 5254578 A 05-10-1993 US 4427137 A 24-01-1984 II 1134362 B 13-08-1986 EF 03128510 A1 19-08-1982 EF 2494390 A1 21-05-1982						
01 3776843 0.1 02-04-1992   EP 0250057 A2 16-03-1988   JP 2512855 B2 21-05-1997   JP 50306906 A 07-04-1988   KR 9601236 B1 24-01-1996   US 5169038 A 08-12-1992 FR 2570139 A1 12-06-1995   EP 0551782 A1 21-04-1996   EP 0551782 A1 21-07-1993   JP 3467629 B2 17-11-2003   JP 5254578 A 05-10-1993   US 4427137 A 24-01-1984 II 1134362 B 13-08-1986   EP 03 128510 A1 19-08-1982   EP 03 128510 A1 19-08-1985   EP 03 128510 A1 19-0			•	AU	7811687 A	
US 4427137 A 24-01-1984 IT 1134362 B 13-08-1986 FR 2249-03-1986 FR 249030 AI 21-05-1987 FR 242930 AI 21-05-1987 FR 242930 AI 21-06-1988 FR 249030 AI 21-06-1988				CA		
JP 2612865 B2 21-05-1997     JP 50176966 A 07-04-1988     KR 9601216 B1 24-01-1996     US 5169038 A 08-12-1992     FR 2670139 A1 12-06-1995     EP 67201591 T2 11-04-1996     EP 0551782 A1 21-07-1993     JP 3467629 B2 17-11-2003     JP 5254578 A 05-10-1993     US 4427137 A 24-01-1984     IT 1134362 B 13-08-1986     FR 2694790 A1 21-05-1982     FR 2694790 A1 21						
US 5169038 A 08-12-1992 FR 2670139 A1 12-06-1995 FR 2670139 D1 24-03-1995 FR 2670139 D1 24-03-1995 FR 6520139 D1 24-03-1995 FR 9520139 T2 11-04-1995 FR 9520139 T2 11-04-1995 FR 952178 A1 21-07-1993 JP 3467629 B2 17-11-2003 JP 5254578 A 05-10-1993 FR 95254578 A 05-10-1993 FR 9520139 A1 21-03-1986 FR 2694390 A1 21-03-1986 FR 2694390 A1 21-03-1985 FR 2694390 A1 21-03-1985 FR 2694390 A1 21-03-1985				J?	2612865 B2	
US 5169018 A 08-12-1992 FR 2470119 A1 12-06-1992 DE 69201591 D1 24-08-1995 DE 69201591 D1 24-08-1995 DE 69201591 D1 24-08-1995 DE 7551782 A1 21-07-1993 JP 3467629 B2 17-11-2003 JP 5254518 A 05-10-1993 DE 3125510 A1 19-08-1982 FR 2494790 A1 21-02-1982 FR 2494790 A1 21-02-1982						
DE 69203591 D1 24-03-1995 D1 69203591 D2 11-04-1996 D1 69203591 T2 11-04-1996 D2 0551762 A1 21-07-1993 D2 0551762 A1 21-07-1993 D2 0551762 A1 21-07-1993 D2 0551762 A1 21-07-1993 D2 0551762 A1 21-020-1998 D2 0551762 A1 21-020-1998 D2 0551762 A1 19-03-1986 D2 0551762 A1 19-03-1986 FR 2494790 A1 21-05-1982				KR	9601236 81	
DE 69203591 D1 24-02-1995 DE 69203591 T2 11-04-1996 EP 0551782 A1 21-07-1993 JP 3467679 82 17-11-2003 JP 5254578 A 05-10-1993 US 4427137 A 24-01-1984 IT 1134362 B 13-02-1985 EP 1326510 A1 19-02-1982 FR 2494790 A1 27-05-1982	05 5169038	_	08-12-1992	FR		12-06-1992
EF 0551782 A1 21-07-1993 JP 3427629 B2 17-11-2003 JP 5254578 A 05-10-1993 US 4427137 A 24-01-1984 IT 1134362 B 13-02-1985 DE 3126510 A1 19-02-1982 FR 2494790 A1 21-05-1982		_				
US 4427137 A 24-01-1984 IT 1134382 B 13-03-1986 FR 2494790 A1 21-03-1984 IT 2135510 A1 19-03-1986 FR 2494790 A1 21-03-1985						
JP 5254578 A 05-10-1993 US 4427137 A 24-01-1994 IT 1134362 B 13-00-1986 DE 3126510 A1 19-00-1982 FR 2494790 A1 21-05-1982						17-11-2003
DE 3126510 A1 19-08-1982 FR 2494390 A1 21-05-1982				JP		05-10-1993
DE 3126510 A1 19-08-1982 FR 2494390 A1 21-05-1982			24-01-1014	77	1134362 R	13-C8-1986
	US 442/13/	^	[4-01-1304			19-08-1982
63 209/335 A ,B 25-U5-1942					2494390 A1	

	MIERONALIONAL SEARCH REPORT		-
		PCT/US 03	/27587
CE	COMPANY'S CONSIDERED TO BE RELEVANT	A	
•	Change of Spinners, with Indicates, where appropriate, of the column principal		Personal to claim to.
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